PATENT
Docket Number 511582003500

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Mary FARIS, et al.

Serial No.: 09/809,638

Filing Date: March 14, 2001

For: 125P5C8: A TISSUE SPECIFIC PROTEIN HIGHLY EXPRESSED IN VARIOUS CANCERS

Examiner: Alana M. Harris, Ph.D.

Group Art Unit: 1642

DECLARATION OF KAREN JANE MEYRICK MORRISON, PH.D.

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Karen Jane Meyrick Morrison, declare as follows:

1. I have a Ph.D. in Pathology from The University of Southampton, U.K. I have worked in the field of histopathology and immunohistochemistry for nearly 25 years. A copy of my curriculum vitae is attached as Exhibit A.

2. I hold the position of Research Scientist at Agensys, Inc., and I run the tissue analysis facility at Agensys. I carry out all procedures associated with histology, including the preparation, processing, cutting, staining and analysis of samples by histological, histochemical and immunohistochemical techniques. These activities include analyses of tissues and cells by bright field microscopy, fluorescence microscopy and computer-aided systems.

3. I have reviewed the specification and claims of the above captioned application. I note that the claims are directed to 125P5C8 polypeptides. Various uses of 125P5C8 polypeptides, as well as uses predicated on immunological responses related to 125P5C8, are clearly available to those in this field based on the disclosure of the current application and knowledge available at the time this case was filed, as I will discuss below.

4. The use of 125P5C8 polypeptide for diagnostic purposes is disclosed throughout the application: For example and without limitation, at page 10, line 9 continued through page 12, line 29; page 26, line 32 continued through page 27, line 14; page 33, line 34 and continued through page 34, line 3; page 37, line 17 continued through page 38, line 14; and Examples 2, 4, 6, 9-10, 12-14, and 17.

5. In addition, the application provides numerous disclosures regarding the use of immunohistochemical techniques. In particular, immunohistochemistry is disclosed in the application as-filed, for example, at page 31 line 30 through page 32 line 2; page 33 lines 14-21; page 34, lines 32-36; page 56, lines 29-32; and, page 69, lines 25-29.

6. Therefore, the application explicitly discloses the use of 125P5C8 as a diagnostic target, as noted in paragraph 4 above. Certain tissues such as prostate express 125P5C8 when normal or malignant. Practical uses in situations where there is expression of 125P5C8 in a tissue whether normal or malignant is a focus of this Declaration.

7. In situations where 125P5C8 is present in malignant tissue, even if it is also in normal tissue, one of skill in the field of histological assessment can perform a variety of analyses such as staining for the 125P5C8 protein. When 125P5C8 is present in both normal and malignant tissue, one can evaluate for any alteration of subcellular localization of the 125P5C8 protein in the malignant relative to normal tissue.

8. By use of any number of well known histological methods, a histologist can determine that a biopsied tissue is, e.g., malignant and that the patient from whom the biopsy was obtained has cancer. These methods can include use of immunohistochemical reagents discussed in paragraph 5 that are directed to 125P5C8. Such histopathology determinations are the basis for vitally important diagnostic and/or prognostic conclusions in a medical or scientific setting. Such diagnoses are not limited to cancer, other meaningful diagnoses based, e.g., on cellular characteristics such as dysplasia or hyperplasia are also possible. A histopathology diagnosis need not be of cancer to be important.

9. Moreover, the ability to make diagnostic decisions, such as described herein, was well known to persons of ordinary skill in the histology and pathology arts at the time the present application was filed. Also well known to such persons was an appreciation of the value of such findings in choosing amongst various treatment approaches.

10. It is important to note that a histopathology diagnosis is made from a biopsy obtained from a specific tissue site or organ. The specific tissue site or organ is disclosed to the scientist in the routine course of requesting an assessment. This is quite different than an artificial situation where a histology or binding event is asserted to be useful as "tissue typing." As I understand this concept of tissue typing, an asserted use is simply information that one tissue has the protein and another tissue lacks the protein. Apparently this fact alone is asserted to give the protein useful meaning.[1]

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[1] Of note, however, a tissue-related conclusion can be important when evaluating a tissue for the possibility of metastases. For example, if an organ does not express a protein, but that organ is a site of metastasis for a particular cancer that does express the protein, the existence of the protein in that organ can indicate the presence of metastases there.

11. The claimed polypeptide and immunogenic compositions thereto are also useful in view of the phenomena of altered subcellular protein localization in disease states. This is a level of information not available from routine tissue staining. Alteration of cells from a normal to a diseased state is correlated with changes in cellular morphology and is often associated with changes in subcellular protein localization/distribution. For example, cell membrane proteins that are expressed in a polarized manner in normal cells can be altered in disease, resulting in distribution of the protein in a non-polar manner over the whole cell surface. The ability to make such diagnostic decisions on the basis of altered subcellular localization was well known to persons of ordinary skill in the histology and pathology arts at the time the present application was filed.

12. The phenomenon of altered subcellular protein localization in a disease state has been demonstrated in several instances, e.g., with Her2 and MUC1 proteins, by use of immunohistochemical means. Accordingly, altered subcellular protein localization in a disease state has been demonstrated with Her2. Normal breast epithelium is either negative for Her2 protein or exhibits only a basolateral distribution whereas malignant cells can express the protein over the whole cell surface (De Potter et al, 1989, International Journal of Cancer, 44; 969-974 (Exhibit B); McCormick et al, 2002, American J. Clinical Pathology, 117: 935-943 (Exhibit C)).

13. MUC1 also demonstrates altered subcellular protein localization in disease states. Normal epithelial cells have a surface only apical distribution of MUC1, along with some supranuclear localization, of the glycoprotein. In contrast, malignant lesions often demonstrate a non-polar and diffuse cytoplasmic staining pattern (Croce, et al, 2003, J. Histochemistry & Cytochemistry 51(6): 781-88 (Exhibit D); Diaz et al, 2001, The Breast Journal, 7; 40-45 (Exhibit

E); Zhang et al, 1998, Clinical Cancer Research, 4; 2669-2676:(Exhibit F); Cao et al, 1997, The Journal of Histochemistry and Cytochemistry, 45; 1547-1557 (Exhibit G)).

14. Alteration in the localization/distribution of a protein in the cell, as detected by immunohistochemical methods, can provide valuable information concerning the favorability of certain treatment modalities. This last point is illustrated by a situation where a protein may be intracellular in normal tissue, but cell surface in malignant cells; the cell surface location makes the cells favorably amenable to antibody-based diagnostic and treatment regimens. Accordingly, the ability to determine whether alteration of subcellular protein localization occurred for 125P5C8 makes the claimed 125P5C8 protein very useful. Use of the claimed compositions allows practitioners to make important diagnostic and therapeutic decisions.

15. Immunohistochemical reagents specific to 125P5C8 are also useful to detect metastases of tumors expressing 125P5C8 when the polypeptide appears in tissues where 125P5C8 is not normally produced. As shown in Figure 6, expression is substantially absent in many tissues and the presence of the polypeptide in these tissues in a subject (e.g., a subject diagnosed with a tumor that expresses 125P5C8) is evidence of metastasis in that individual.

16. In summary, claimed 125P5C8 polypeptides and antibodies resulting from immune responses thereto are useful in a variety of important contexts, uses supported by the specification as-filed.

17. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are

punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at Santa Monica, California, on 10 July 2003.

Karen Jane Meyrick Morrison

KAREN JANE MEYRICK MORRISON, PH.D. DECLARATION EXHIBITS:

Exhibit A	Karen Morrison *curriculum vitae*
Exhibit B	De Potter et al, 1989, International Journal of Cancer, 44; 969-974
Exhibit C	McCormick et al, 2002, American J. Clinical Pathology 117: 935-943
Exhibit D	Croce et al, 2003, The Journal of Histochemistry & Cytochemistry, 51(6):781-788
Exhibit E	Diaz et al, 2001, The Breast Journal, 7; 40-45
Exhibit F	Zhang et al, 1998, Clinical Cancer Research, 4; 2669-2676
Exhibit G	Cao et al, 1997, The Journal of Histochemistry and Cytochemistry, 45; 1547-1557